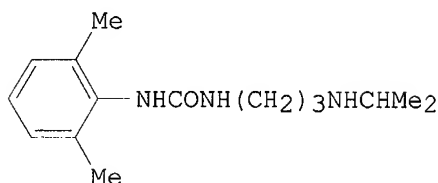


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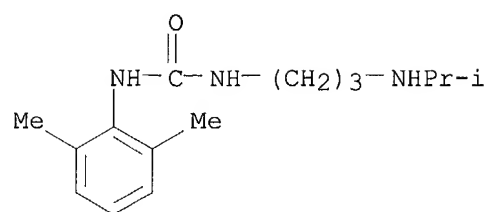
ACCESSION NUMBER: 110:185631 CA
TITLE: Frequency- and voltage-dependent effects of recainam on the upstroke velocity of action potential in rabbit ventricular muscle
AUTHOR(S): Kamiya, Kaichiro; Takikawa, Reiko; Singh, Bramah N.
CORPORATE SOURCE: Sch. Med., UCLA, Los Angeles, CA, USA
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GI



AB The effects of recainam (Wy 42,362) (I) on transmembrane action potentials were examd. in isolated rabbit right ventricular papillary muscles. Recainam (3 .times. 10⁻⁵ to 3 .times. 10⁻⁴ M) caused a concn.-dependent decrease in the .ovrhdot.Vmax of the action potential. At 3 .times. 10⁻⁴ M, there was a slight decrease in the amplitude of the action potential. The resting potential and the action potential duration were not affected. Use-dependent block of .ovrhdot.Vmax was tested over a wide range of pacing frequencies (0.1-3.0 Hz). At 1.0 Hz, recainam 10⁻⁴ M produced exponential decreases in .ovrhdot.Vmax with a rate const. of 0.17 per action potential and 3.98% redn. at steady state. This use-dependent block was augmented at the higher stimulation frequencies. The time const. for the recovery of .ovrhdot.Vmax from use-dependent block (offset) was 17.2 s. In papillary muscles depolarized with 10 mM [K⁺]O, the use-dependent block was augmented but tonic block and the rates of onset and offset of the use-dependent block were similar to those in normally polarized prepns. in 4 mM [K⁺]O. The curves relating membrane potential and .ovrhdot.Vmax in prepns. stimulated at a low frequency (0.01 Hz) were not shifted by 10⁻⁴ M recainam. These findings suggest that recainam is a specific Na-channel blocker and has kinetically slow but potent affinity for the channel during action potentials. This selective binding during action potential was further augmented by depolarization and is likely to play a significant role in the control of ventricular arrhythmias by the drug.

IT 74738-24-2, Wy 42362
RL: BIOL (Biological study)
(ventricular arrhythmia **inhibition** by, mechanism of)
RN 74738-24-2 CA
CN Urea, N-(2,6-dimethylphenyl)-N'-[3-[(1-methylethyl)amino]propyl]- (9CI)
(CA INDEX NAME)

10/019,652



IT **74738-24-2**, Wy 42362

RL: BIOL (Biological study)

(ventricular arrhythmia **inhibition** by, mechanism of)